Potentially inappropriate medications prescribed for older persons: A study from two teaching hospitals in Southern India

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Abstract:

BACKGROUND: Potentially inappropriate medications (PIMs) are a major concern in geriatric care. The primary objective of our study was to assess the prevalence of PIMs prescribed for older persons attending outpatient setting of two teaching hospitals in Kerala state in South India, where the population is aging.

MATERIALS AND METHODS: A cross-sectional study was carried out in two teaching hospitals in Kerala. Four hundred consecutive outpatient medical records of patients aged 65 years and above were selected. The current medications of the patients were analyzed to identify PIMs by the Beers criteria 2015. Polypharmacy and hyperpolypharmacy were defined as 5–9 medications and ≥ 10 medications, respectively. Chi-square test was done to identify demographic variables and the pattern of health-care facility use associated with PIM prescription. Binary logistic regression was performed to adjust for confounding associations.

RESULTS: The prevalence of PIMs prescription was 34.0% (95% confidence interval: 29.4%–38.6%) and that of polypharmacy and hyperpolypharmacy was 45.8% and 13.5%, respectively. The common PIMs were proton-pump inhibitors, benzodiazepines, peripheral α-1 blockers, and first-generation antihistamines. Inpatient admission, visits to the emergency department, multiple diagnoses, polypharmacy, and hyperpolypharmacy were associated with PIM prescription ($P < 0.05$). Age, gender, number of outpatient visits, and specialist consultation were not associated with PIM prescription. Polypharmacy (adjusted odds ratio [aOR] =2.11) and hyperpolypharmacy (aOR = 5.55) had independent association with PIM prescription ($P < 0.05$).

CONCLUSION: PIM prescription appears to be common in teaching hospitals in Kerala. Polypharmacy and hyperpolypharmacy in older people should trigger a review of medication to reduce the use of PIM.

Keywords:

Beers criteria, geropharmacology, hyperpolypharmacy, polypharmacy, potentially inappropriate medications

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Introduction

The population of Kerala, the southernmost state in India, is aging faster than the rest of the country. The aged population (defined as age 60 years and above in India) in the state grew from 5.8% in 1961 to 12.3% in 2011 compared to 5.6% in 1961 to 8.3% in 2011 as shown in the national statistics.[1] In this study, old age was defined the age of 65 years and above as it is in most developed countries.[2] With this demographic shift, health-care professionals in Kerala come across an increasing number of older persons in their day-to-day clinical practice. Older persons have diminished

physiological reserve, making them vulnerable to the adverse effects of altered pharmacodynamics and pharmacokinetics.[3] They have double the risk of hospitalization on account of adverse drug reactions,[4] and drug-induced iatrogenesis in older persons is known to be prevalent in all health-care settings.[5] It was estimated that preventable medication-related adverse incidents and deaths cost $11 billion in Canada annually.[6]

Multimorbidity, defined as the coexistence of two or more chronic conditions, is common in old age,[7] and more medications may be needed to treat them. The use of multiple medicines is commonly referred to as polypharmacy, the most common numerical definition of which is the use of five or more medications.[8] The appropriateness of polypharmacy has to be evaluated under different criteria such as potentially inappropriate medications (PIMs), medication underuse, and medication duplication.[9]

PIMs are medications whose risks outweigh benefits owing to the physiology of old age, drug–drug interactions, or drug–disease interactions.[10] They are to be avoided or used with caution or their dose optimized.[10] The Beers criteria were developed by a panel of experts by the Delphi method as a simple tool to identify PIMs.[10] The Beers criteria apply to the age group of 65 years and above and in the 2015 update are a list of medications by therapeutic category, medications to be avoided in specific diseases or syndromes, medications to be used with caution, clinically important drug–drug interactions, and a list of medications whose doses are to be adjusted according to kidney function.[10] The Beers criteria are intended to be used as an evidence-based tool to help in decision-making, while prescribing for older adults.[10] A systematic review concluded that inappropriate medications according to the Beers criteria were associated with an adverse impact on the health care of older adults within the community.[11]

There are no studies from settings in Kerala using the Beers criteria 2015. This study's aim was to assess the prevalence of PIM prescriptions and associated factors among older patients attendinng two private teaching hospitals in Kerala state.

Materials and Methods

This was a hospital record-based cross-sectional study conducted in the outpatient departments (OPDs) of general medicine in two private, not-for-profit teaching hospitals in Kerala. Hospital records of patients aged 65 years and above were included in the study, with no exclusion criteria.

The list of hospital patients who attended general medicine OPD from the first of January 2016 was obtained from the medical records department. Consecutive sampling was done till the sample size was attained. Two hundred hospital records were retrieved for analysis, from each center over a period of 6 months. The sample size estimated was 398 for an expected prevalence of 30%,[12] relative precision of 15%, and α-error of 5%.

A manual review of patient charts with a structured pilot-tested data extraction form was conducted as these centers did not have electronic medical records. A structured data extraction form was developed and standardized after pilot testing and review in both centers. The chart reviews were done by the resident investigators of the institutions over a period of 1 year. The latest medications prescribed were analyzed according to the 2015 Beers criteria.[10] The data were de-identified by coding to maintain confidentiality. The variables included in the form were as follows: age, sex, diagnoses, medications prescribed with dose and schedule at the latest visit, specialist consultations, number of hospital admissions, number of emergency department (ED) visits, and the number of OPD visits in the previous 6 months.

The prescriptions were analyzed against drug list by organ system and therapeutic category, list of drug-drug interactions and list of drug–syndrome interactions in the Beers criteria 2015.[10] The optimum number of medications was defined as less than five, polypharmacy was defined as the use of 5–9 medications, and hyperpolypharmacy was defined as the use of ten or more medications.[13]

The data were entered into Epi Info version 7.1.4.0 (developed by Centers for Disease Control and Prevention (CDC), Atlanta, Georgia, United States)and analysis was done in R software version 3.1.3 (developed by (R foundation) The prevalence of PIM use with 95% confidence intervals (CIs) was calculated. Associations of PIM use with demographic variables, polypharmacy, hyperpolypharmacy, and characteristics of health-care facility utilization were analyzed by Chi-square test. $P < 0.05$ was regarded as statistically significant. Binary logistic regression model included variables which had $P < 0.10$ in bivariate analysis. Ethical approval with a waiver of written informed consent had been obtained from the Institutional Review Board/Ethics Committees of both centers.

Results

In this study, 400 patient records were analyzed. The mean age of the patients was 73.6 years (standard deviation: 6.7 years); 36.7% were 75 years and above and

63.3% were aged between 65 and 74 years, and 52.3% were females. Of these patients, 29.5% had had five or more OPD visits, 42.2% had two to four OPD visits, and 35.7% had visits to specialties other than general medicine, 16.8% had attended the ED, and 21.5% had been admitted for inpatient care in the previous 6 months [Table 1]. Of the participants, 19.2% had one, 23% had two, 27.5% had three, and 30.3% had four or more disease conditions. A list of the most common diseases is shown in Table 2. The prevalence of polypharmacy was 45.8% (95% CI: 40.9–50.7) and hyperpolypharmacy was 13.5% (95% CI: 10.2–16.8).

According to the Beers criteria 2015, the prevalence of PIMs was 34.0% (95% CI: 29.4–38.6). Of the 136 patients on PIMs, 108 (79.4%) had one, 23 (16.9%) had two, and 5 (3.7%) had three PIMs. Of 136 patients on PIMs, the most common PIM therapeutic category was prolonged use (>8 weeks) of proton-pump inhibitors (PPI) (52.9%), followed by benzodiazepines (16.9%), peripheral alpha-1 blockers (11.7%), and first-generation antihistamines (8.1%). The complete list of PIMs identified is shown in Table 3. Four patients had potentially inappropriate drug–drug interactions (benzodiazepines with more than two psychoactive drugs) and three patients had potentially inappropriate drug–disease interaction (dicyclomine in a patient with benign prostatic hypertrophy and nonsteroidal anti-inflammatory drugs in two patients with congestive cardiac failure).

The factors such as inpatient admission in the previous 6 months (odds ratio [OR] =1.64, 95% CI: 1.01–2.67), visits to the ED in the previous 6 months (OR = 1.87, 95% CI: 1.09–3.19), more than four diagnosed diseases (OR = 2.37, 95% CI: 1.52–3.69), polypharmacy (OR = 2.54, 95% CI: 1.56–4.13), and hyperpolypharmacy (OR = 6.96, 95% CI: 3.55–13.66) were found to be associated with the prescription of PIM ($P < 0.05$), as shown in Table 4. Age, gender, the number of OPD visits, and specialist consultation were not associated with PIM prescription. The binary logistic regression with the variables with $P < 0.10$ in bivariate analysis showed that only polypharmacy (aOR = 2.11, 95% CI: 1.24–3.63) and hyperpolypharmacy (aOR = 5.55,

Table 1: Pattern of facility utilization in the hospital by the older patients during past 6 months (*n*=400)

Hospital facility utilization	Number (%)
Number of visits to OPD	
Once	113 (28.3)
Two to four times	169 (42.2)
Five or more times	118 (29.5)
Number of specialist departments consulted	
One (general medicine)	257 (64.3)
Two	102 (25.5)
Three	27 (6.7)
Four or five	14 (3.5)
Visit to ED	67 (16.8)
Admitted for inpatient care	86 (21.5)

OPD=Outpatient department, ED=Emergency department

Table 2: Major diagnoses of the patients (*n*=400)

Diagnosis	Number (%)
Chronic diseases	
Hypertension	256 (64.0)
Diabetes mellitus	199 (49.7)
Dyslipidemia	99 (24.7)
Coronary artery disease	77 (19.2)
Chronic obstructive pulmonary disease	74 (18.5)
Hypothyroidism	24 (6.0)
Cerebrovascular accidents	24 (6.0)
Chronic kidney disease	23 (5.7)
Benign prostatic hypertrophy	21 (5.2)
Acute diseases	
Lower respiratory tract infection	32 (8.0)
Acute febrile illness/upper respiratory tract infection	22 (5.5)

Table 3: Potentially inappropriate medications prescribed for older persons by therapeutic category (*n*=136)

PIM therapeutic category	Drugs	Number (%)
PPI (>8 weeks)	Omeprazole, pantoprazole, rabeprazole, esomeprazole	72 (52.9)
Benzodiazepines	Alprazolam, clonazepam, lorazepam	23 (16.9)
Peripheral alpha-1 blockers	Prazosin	16 (11.7)
First-generation antihistamines	Chlorpheniramine, diphenhydramine, hydroxyzine	11 (8.1)
Nonsteroidal anti-inflammatory drugs	Diclofenac, aceclofenac, etodolac, ibuprofen	10 (7.4)
Central alpha-blockers	Clonidine, reserpine	8 (5.9)
Second-generation antipsychotics	Risperidone	4 (2.9)
Anticholinergic antiparkinsonian	Trihexyphenidyl	4 (2.9)
Anticholinergic antispasmodic	Dicyclomine	4 (3.0)
Tricyclic antidepressants	Amitriptyline Nortriptyline	3 (2.2)
Endocrine	Glyburide/glibenclamide	3 (2.2)
Benzodiazepine agonist hypnotic	Zolpidem	3 (2.2)
Cardiovascular drug for atrial fibrillation	Digoxin	3 (2.2)
Barbiturates	Phenobarbitone	1 (0.7)
Skeletal muscle relaxants	Metaxolone	1 (0.7)

Total exceeds 100% as there were patients on more than one PIM. PIM=Potentially inappropriate medication, PPI=Proton-pump inhibitors

95% CI: 2.53–12.49) had independent association with PIM prescription [Table 5].

Discussion

The prevalence of PIM prescriptions was 34.0%, polypharmacy was 45.8%, and hyperpolypharmacy was 13.5%. The gender distribution was nearly equal, with one-third aged 75 years and above and four-fifths who had multimorbidity (defined as more than one diagnosis). The most common PIMs were PPI, benzodiazepines, peripheral alpha-1 blocker, and first-generation antihistamines. Inpatient admissions, visits to ED, more than four diagnosed diseases, polypharmacy, and hyperpolypharmacy were associated with PIM prescription, among which the latter two were found to be independently associated.

Reports of prevalences of PIMs from various parts of India are as followed. Rakesh KB *et al*. from a tertiary care centre OPD setting in Karnataka found a low prevalence

of PIMs (8.4%) by 2015 Beers criteria.[14] A previous study in Kerala, using a modified 2012 Beers criteria, reported the prevalence of PIMs as 29.5% of patients attending a geriatric clinic setting for the first time.[12] Other studies in OPD settings using the 2012 Beers criteria showed a prevalence range of PIMs of 17.3%–21.8%.[13-15] Pradhan *et al*. reported benzodiazepines as the most common PIM.[15] Manjaly *et al*. reported that the most common PIMs belonged to the cardiovascular category, followed by benzodiazepines and tricyclic antidepressants.[16] Kanagasanthosh *et al*. reported drugs in the cardiovascular category and Non-Steroidal Anti Inflammatory Drugs as the most common PIMs.[17] In our study, the most common PIMs were PPIs, which are a new addition to the 2015 Beers criteria and also may account for the higher prevalence in our study compared to previous studies which used the 2012 Beers criteria.[10] A study in an inpatient setting in Uttarakhand using the 2015 Beers criteria reported the prevalence of PIMs as 32.1%.[18] In their study, the most common PIMs belonged to the cardiovascular

Table 4: Factors associated with prescription of potentially inappropriate medications for older patients (*n*=400)

Variables	Category	PIMs N (%)	No PIMs N (%)	OR (95% CI)	P-Value
Age (years)	65-74	85 (33.6)	168 (66.4)	0.95 (0.62-1.46)	0.82
	≥75	51 (34.7)	96 (65.3)		
Gender	Male	66 (34.6)	125 (65.4)	1.05 (0.69-1.58)	0.82
	Female	70 (33.5)	139 (66.5)		
Inpatient admission (past 6 months)	Yes	37 (43.0)	49 (57.0)	1.64 (1.01-2.67)	0.04
	No	99 (31.5)	215 (68.5)		
Number of OPD visits (past 6 months)	≥5	50 (42.4)	68 (57.6)	1.70 (0.99-2.94)	0.05
	2 - 4	52 (30.8)	117 (69.2)	1.03 (0.62-1.73)	0.90
	1	34 (30.1)	79 (69.9)	1	-
Specialist consultation (past 6 months)	Yes	57 (39.9)	86 (60.1)	1.49 (0.97-2.23)	0.06
	No	79 (30.7)	178 (69.3)		
Visit to ED (past 6 months)	Yes	31 (46.3)	36 (53.7)	1.87 (1.09-3.19)	0.02
	No	105 (31.5)	228 (68.5)		
Number of diagnoses	>3	58 (47.9)	63 (52.1)	2.37 (1.52-3.69)	<0.001
	≤3	78 (28.0)	201 (72.0)		
Number of medications	Hyperpolypharmacy (≥10)	34 (63.0)	20 (37.0)	6.96 (3.55-13.66)	<0.001
	Polypharmacy (5-9)	70 (38.3)	113 (61.7)	2.54 (1.56-4.13)	<0.001
	Optimum (<5)	32 (19.6)	131 (80.4)	1	-

OPD=Outpatient department, ED=Emergency department, OR=Odds ratio, CI=Confidence interval, PIMs=Potentially inappropriate medications

Table 5: Factors independently associated with prescription of potentially inappropriate medications for older persons (*n*=400)

Variables	Category associated with PIMs	AOR (95% CI)	P-Value
Inpatient admissions (past 6 months)	Yes versus no	1.36 (0.77-2.38)	0.29
Number of OPD visits (past 6 months)	Five or more versus single	1.17 (0.62-2.21)	0.61
	Two to four versus single	0.95 (0.53-1.70)	0.85
Departments visited (past 6 months)	General medicine only versus visit to specialty as well	1.08 (0.66-1.75)	0.74
Visit to ED (past 6 months)	Yes versus No	1.34 (0.74-2.40)	0.33
Number of diseases	More than three versus up to three	1.15 (0.67-1.97)	0.59
Number of medications	Hyperpolypharmacy (≥10) versus optimum (<5)	5.55 (2.53-12.49)	<0.001
	Polypharmacy (5-9) versus optimum (<5)	2.11 (1.24-3.63)	0.006

OPD=Outpatient department, AOR=Adjusted odds ratio, CI=Confidence interval, PIMs=Potentially inappropriate medications, ED=Emergency department

Table 6: Reports on the prevalence of potentially inappropriate medications by 2015 Beers criteria from various parts of the globe

Source	Setting	Country	Age group (years)	Prevalence of PIMs %
Sarwar *et al*., 2018[22]	Outpatient	Pakistan	≥65	36.4
Saka *et al*., 2018[23]	Inpatient	Nigeria	≥60	32.1
		South Africa	≥60	30.1
Grina and Briedis 2017[24]	Insurance claims	Lithuania	≥65	25.9
Bala *et al*., 2018[25]	Community dwelling	New Zealand	≥65	24.7
Patel *et al*., 2018[26]	Mobile Medicare clinics	US, North California	≥65	29.0
Alhawassi *et al*., 2019[27]	Outpatient	Saudi Arabia	≥65	57.6
Zhang *et al*., 2017[28]	Inpatient	China	≥65	53.5
Chiapella *et al*., 2018[29]	Community pharmacies	Argentina	≥65	72.7

PIMs=Potentially inappropriate medications

category (central alpha-blocker and peripheral alpha-1 blocker). PPIs (prescribed for >8 weeks) were not reported[18] probably because the study only looked at the inpatient period which would not be enough to ascertain duration for which PPI would be taken. Two other studies at inpatient settings used the 2012 Beers criteria, and the prevalence for the two studies was 33.2% and 23.5%, respectively.[19,20] A study in a community setting using the 2012 Beers criteria had the prevalence of PIMs as 17.5%; the most common PIMs are analgesics, antidepressants, and vasodilators.[21]

Table 6 shows various studies with the prevalence of PIMs according to the 2015 Beers criteria from various countries. Studies from Pakistan, Nigeria, and South Africa reported the prevalence of PIMs comparable to our study.[22,23] Studies from Lithuania, New Zealand, and the United States show a slightly lower prevalence of PIMs.[24-26] Studies from Saudi Arabia, China, and Argentina reported a higher prevalence of PIMs.[27-29] However, the differences in the study settings may limit the value of comparison. The average prevalence of PIMs was 58% for community patients and 55.5% for hospitalized patients in a systematic review of 19 studies.[30] PPI was reported as the most common PIMs in our study and a few others.[28,31,32] It is known that PPIs are being misused and overused worldwide.[33] In the United States of America, PPI prescriptions that were guidelines compliant were only 50% in academic hospitals and 29% in nonacademic hospitals.[34]

The high prevalence of PIMs in our study may be attributed to the profile of patients who generally have multiple morbidities and attend teaching hospital clinics. The assumption is that teaching hospitals are abreast with the latest evidence-based medical practice. The use of PIMs could be higher in nonacademic settings. The study identified some opportunities for interventions. Medication review should be conducted for patients on hyperpolypharmacy and polypharmacy, patients discharged after a hospital admission, and those who attend the ED. The current knowledge and practice of clinicians in the pharmacological management of older patients in these settings need to be explored and further interventions planned accordingly. Physician education programs may be effective in preventing the prescription of PIMs.[35] Deprescribing is challenging, but[36] could be done effectively,[37] and would be acceptable to patients.[38]

The study had involved two private teaching hospitals: one from Central Kerala and the other from South Kerala. The results may not be applicable to other settings such as government teaching hospitals and nonacademic settings. The analysis was limited to three tables in the Beers criteria. Data on over-the-counter drugs, medications prescribed from other hospitals, and medications in other systems of medicines which the patient may be concurrently taking were not captured in the study. Hence, there is a possibility that the prevalence of PIMs reported in this study may be an underestimation.

Conclusion

Polypharmacy and PIMs are prevalent in teaching hospitals of Kerala. The most common PIM was PPIs, followed by benzodiazepines, peripheral α-1 blockers, and first-generation antihistamines. Polypharmacy or hyperpolypharmacy shall trigger a medication review. Additional time points for medication review can be after discharge from a hospital admission and a visit to the ED.

Conflicts of interest
There are no conflicts of interest.

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